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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/088,951	06/02/98	CHEEVER	M 920010.535

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EXAMINER	
UNGAR, S	
ART UNIT	**PAPER NUMBER**
1642	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/088,951	Applicant(s) Cheever et al
	Examiner Ungar	Group Art Unit 1642

☒ Responsive to communication(s) filed on *Sep 27, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-12* is/are pending in the application.

Of the above, claim(s) *2-6 and 10* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 7-9, 11, and 12* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *10*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. The Election filed September 27, 1999 (Paper No. 7) in response to the Office Action of July 21, 1999 (Paper No. 5) and the Supplemental Response to Election Requirement filed December 27, 1999 (Paper No. 9) in response to the Communication of December 6, 1999 (Paper No. 8) are acknowledged and have been entered. Claims 1-12 are pending in the application and Claims 2-6, and 10 as well as claims 11 and 12 as they are drawn to inventions other than the elected species have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 1, 7-9 and 11-12, as drawn to the elected species, are currently under prosecution.

2. The responses (Paper Nos. 7 and 9) to the restriction requirement of July 21, 1999 have been received. Applicant has elected the species of PAP as the single species, wherein the species is organ-specific or tissue specific associated with tumor cells and this is a species of an antigen. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a).

Specification

3. The specification on page 1 should be amended to reflect the status of the parent application serial number 60/048,406 and to recite that "This application claims benefit to provision application 60/048,406, filed June 3, 1997, now abandoned."

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

5. Claims 1, 7-9 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a foreign protein or protein homologous to an antigen. The specification teaches that a protein or peptide as "foreign" when it is not identical to that in the individual but nevertheless homologous to an individual's self tumor antigen or portion thereof (p. 9, lines 10-11. Further, although not limiting, the specification defines a foreign protein as "homologous" when it is not identical to human self tumor antigen (p. 10, lines 2-4). Finally the specification teaches that "As used herein a "foreign protein homologous to a human self antigen" means a protein that is homologous, but not identical in entire amino acid sequence to a human self tumor antigen." (See p. 10, lines 5-10). The specification teaches that generally a foreign protein will possess at least about 50% sequence homology to the self tumor and defines sequence homology as either identical amino acids at the same positions in the sequence (i.e. sequence identity) or conservative substitutions of amino acids at the same positions in the sequence (p. 10, lines 8-

11). One cannot extrapolate the teaching of the specification to the enablement of the claims because there is no limiting teaching as to the extent of "homology" being claimed and there is no teaching of how to make the foreign homologous proteins or peptides so that they will function as claimed and no teaching of where or how to isolate these proteins or peptides if they are found in nature. The claims as written read on proteins and peptides native to the "individual" that have been mutated or altered in a fashion that would render them "not identical" to the native antigen. However, the specification does not teach what positions of the protein must be retained that will result in a foreign homologous antigen having useful immunogenic activity that will function as claimed or what portions of a protein, i.e. a peptide, must be used in order to function as claimed. Further, said foreign antigens read on molecules which have been subjected to deletions, truncations, additions as well as substitutions of a multitude of tumor antigens. However, applicant has not enabled all of these types of modified proteins because it has not been shown that these modified proteins are capable of functioning as that which is being disclosed. The single example of a rat homolog of PAP is not sufficient enablement for the claims. Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that

while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining structure/function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). Further, it is well known in the art, as taught by Herbert et al (The Dictionary of Immunology, Academic Press, London, 1996, p. 58) that antibodies bind in an approximate three-dimensional fit with an epitope thus the three dimensional structure of the protein molecule to which an antibody binds is essential for antibody binding (p. 58). Finally, US Patent No. 5,952,362 specifically teaches that an antigen will be a protein that includes the amino acid sequence of the antigen or epitope (col 3, lines 23-26). Clearly the effects of differences in the amino acid sequence between foreign homologous antigens and self-tumor antigens would be expected to result in differences in structure and the effect of these differences on the formation of antibodies that could bind self-tumor antigens can not be predicted. The specification provides insufficient guidance with regard to these issue and provides no working examples which would provide guidance to one skilled in the art and without knowing how to make the foreign homologous antigens, one would clearly not know how to use the invention or practice the claimed methods with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

6. Claims 7-9 and 11-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7-9 and 11-12 are indefinite because claims 7 recites "wherein said antigen or said antigen portion is an.....antigen associated with tumor cells or a portion of the antigen". Further, claim 8 recites "or a portion of the antigen". The claims are confusing because it is not possible to determine the meaning of the words "or a portion of the antigen". Does this refer to an antigen which is associated with a portion of the antigen and if so, which antigen is being referred to?

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

8. Claims 1, 7-9 and 11-12 are rejected under 35 U.S.C. § 102(e) as being anticipated by US Patent No. 5,925,362.

The claims are drawn to a method of eliciting or enhancing an immune response to a human self tumor antigen comprising immunizing a human with a foreign protein homologous to said antigen or with a foreign peptide homologous to

a portion of said antigen wherein said antigen or antigen portion is an organ-specific or tissue specific antigen associated with tumor cells, wherein said antigen is an antigen associated with prostate cancer, wherein said antigen is PAP, wherein said foreign protein or foreign peptide is in a pharmaceutically acceptable carrier or diluent wherein an adjuvant is additionally used.

It is noted that although not limiting, the specification defines a protein or peptide as "foreign" when it is not identical to that in the individual but nevertheless homologous to an individual's self tumor antigen or portion thereof (p. 9, lines 10-11. Further, although not limiting, the specification defines a foreign protein as "homologous" when it is not identical to human self tumor antigen (p. 10, lines 2-4). Finally the specification teaches that "As used herein a "foreign protein homologous to a human self antigen" means a protein that is homologous, but not identical in entire amino acid sequence to a human self tumor antigen." (See p. 10, lines 5-10).

US Patent No. 5,925,362 teaches that prostate cancer is the most common malignancy among males in the US and is refractive to surgery and radiation treatment (col 1, lines 30-40) and that the instant invention concerns the use of prostate antigens or their representatives in vaccines to produce an immune response to treat prostate cancer (col 2, lines 30-32). US Patent No. 5,925,362 teaches vaccines comprising tumor antigens capable of eliciting an immune antitumor response to prostate tumors and that such vaccines are selected from the group including human PSA (see abstract) and PAP (col 3, lines 64-66 and col 4, lines 12-15) or peptides thereof (col 3 lines 14-33), both of which are prostate-specific antigens associated with prostate cancer (col 3, lines 64-66 and col 4) and further

teaches that when administered as part of a fusion protein the antigen is administered in the presence of suitable excipients (col 7, lines 35-40) and are administered in a pharmaceutically acceptable carrier (col 8, lines 42-45) wherein an adjuvant is additionally used (col 7, lines 5 and 57-67). Further, the specification teaches that the antigen may be prepared as a fusion protein containing amino acid sequences heterologous to the amino acid sequence of interest and that construction of such fusion proteins is common in recombinant production in order to stabilize the product. The fusion product is useful in the vaccine, especially when additional heterologous amino acid sequence supplies an immunogenicity enhancing property (col 6 lines 16-38). Finally, US Patent No. 5,925,362 teaches the administration of the vaccine for eliciting an immune antitumor response to prostate tumors (col 8, line 15-col 9 line 20).

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
March 3, 2000